REMARKS

The Office Action mailed December 17, 2002, has been received and its contents carefully noted. The pending claims are claims 13-25. Claims 13-18 were withdrawn from consideration. Claims 19-25 were rejected. By this amendment, claims 13-18 have been canceled, claim 19 has been amended, and claims 26-31 have been added. Support may be found in the specification and claims as originally filed. No statutory new matter has been added. Reconsideration is respectfully requested.

Rejection under 35 U.S.C. §112, second paragraph

The Examiner rejected claims 19-25 under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter in the present invention. Specifically, the Examiner deemed that claim 19 recites the terms "stitching agent" and that neither the specification nor the claims teach one of ordinary skill in the art the meaning of "stitching agent".

The Applicant respectfully submits that "stitching agent" is a translation error that occurred when the Russian priority document was translated from Russian into English. Applicant submits that one skilled in the art that is capable of translating from Russian to English would understand that the Russian term should have been translated to "linking agent" or "binding agent". Therefore, Applicant has amended the claims such that "stitching agent" is changed to "linking agent". The specification provides glutaric dialdehyde as an example of the linking agent. One skilled in the art would clearly understand that "stitching agent" in combination with the teachings of the specification, i.e. glutaric dialdehyde, refers to a "linking agent" or a "binding agent". Therefore, the specification provides sufficient written description support for correction of the translation error.

As one skilled in the art would clearly understand the scope and meaning of "linking agent", the rejection under 35 U.S.C. 112, second paragraph, should properly be withdrawn.

Rejection under 35 U.S.C. § 103(a)

The Examiner rejected claims 19-25 under 35 U.S.C. 103(a) as being unpatentable over Morenkova (Derwent abstract, ACC-NO 1997-041104, alternatively '788 patent) in view of Cho *et al.* (U.S. Patent No. 5,665,700). Specifically, the Examiner deemed that Morenkova teaches

insulin-containing medicine for peroral use comprising a stitching agent (i.e. glutarite dialdehyde), insulin, erythrocytes which are excreted from animal or humans and does not teach gelatin contained within an insulin-containing medicine. The Examiner deemed that Cho *et al.* beneficially teach gelatin contained within an insulin preparation for packing purposes. Thus, the Examiner deemed that it would have been obvious to one of ordinary skill in the art to modify Morenkova to include gelatin as beneficially disclosed by Cho et al. for packaging purposes of an insulin-containing medicine.

Applicant respectfully submits that the Examiner cites Morenkova as disclosing a method for preparing the insulin preparation by incubating insulin with erythrocytes in the ratio of 1-4:10. However, this ratio should properly be 1-4:100. See Morenkova, '788 patent first page. Applicant directs the Examiner's attention to the fact that the original claim 7 of application PCT/RU99/00463 had a typographical error which remained in the English language translation. Specifically, the concentration of the linking agent was incorrectly indicated as 0.5-0.35%. The correct concentration is 0.05-0.35. The support for this can be found in the specification. See, for example, page 5, lines 10-15.

Applicant respectfully submits that Morenkova discloses 0.15-0.25% of glutaric dialdehyde in the final concentration of the insulin preparation. The present invention as claimed comprises 0.05-0.15% of the linking agent in the final composition.

The difference in the concentrations of the linking agent is significant. Specifically, glutaric dialdehyde is known to be toxic. Thus, lower concentrations are desirable because of reduced toxicity. However, it was unknown until the present invention whether concentrations less than 0.15% could still link erythrocytes and insulin. Unexpectedly, Applicant discovered that linking agents in concentrations of less than 0.15% are sufficient to link erythrocytes and insulin. In support, 0.05% of the linking agent was sufficient. Specifically, an insulin-containing medicament comprising 5-10 wt% insulin and 100 wt% erythrocytes was tested.

The insulin-containing medicaments containing ratios of insulin to erythrocytes of 5:100; 8:100 and 10:100 (using in an incubation medium a linking agent in the final concentration of 0.05%) were administered to adult male mice having a mass of 20 grams through a probe in the volume of 0.2 ml. The animals received 2.0-2.5 units of insulin in the insulin-containing medicament.

Diabetes was induced with streptozotocyn. The results are shown in the following Table:

Animal groups	**Animal number**	**Glucose in blood mM/1 ---------- average fluctuation limits**	**% reduction to norm**
Without insulin-containing medicament (norm, 100%)	10	15.10 14.71±4.5	
Insulin-containing medicament according to invention (insulin:erythrocytes 5:100)	10	5.28 4.92±2.5	65
Insulin-containing medicament according to invention (insulin:erythrocytes 8:100)	10	5.58 7.10±2.9	63
Insulin-containing medicament according to invention (insulin:erythrocytes 10:100)	10	5.43 5.92±2.5	64

As seen from the data provided above, all the preparations have similar activity. Thus, insulin preparations containing a ratio of insulin:erythrocytes of 5-10:100 and a 0.05% concentration of glutaric dialdehyde 0.05% substantially reduced glucose in patients.

Nowhere does the prior art teach or suggest that lower concentrations of linking agents may be used in insulin preparations without losing activity. As one skilled in the art would not be motivated to make and use the claimed compositions for fear of reduced activity, the rejection under 35 U.S.C. 103(a) should properly be withdrawn.

Request for Interview

Applicant respectfully requests either a telephonic or an in-person interview should there be any remaining issues.

Extension of Time

A Petition for an Extension of Time for one (1) month under 37 C.F.R 1.136 and the appropriate fee are submitted herewith to extend the time for responding to the Office Action to April 17, 2003.

Conclusion

Accordingly, in view of the foregoing amendments and remarks, the Examiner is respectfully requested to reconsider and withdraw the rejection of the claims to allow these claims and to find this application to be in allowable condition.

Respectfully submitted,

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